UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,385	09/09/2004	Teizo Yoshimura	4239-64104-02	8908

36218 7590 06/18/2009

KLARQUIST SPARKMAN, LLP
121 S.W. SALMON STREET
SUITE #1600
PORTLAND, OR 97204-2988

EXAMINER	
LEAVITT, MARIA GOMEZ	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
06/18/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/507,385	YOSHIMURA, TEIZO	
	Examiner	Art Unit	
	MARIA LEAVITT	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-13,15-33 and 46-59* is/are pending in the application.

4a) Of the above claim(s) *1-9,15,16,26-33 and 46-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-13,17-25 and 55-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. Status of claims. Applicant's response to the Office Action of 11-14-2008 has been entered. Claims 1-9, 11-13, 15- 33 and 46-59 are currently pending. Claims 12, 13, 20, and 57 have been amended, claims 10 and 14 have been cancelled, and claims 58 and 59 have been added by Applicants' amendment filed on 04-14-2009. Claims 1-9, 26-33 and 46-54 were previously withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 23-25 were previously rejoined with claims 11-22 in the office action filed on 11-14-20008. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.
3. The examiner acknowledges receiving the following documents: a Declaration under 37 C.F.R. § 1.132 signed by Dr. Teizo Yoshimura on April 13, 2009 and filed on April 14, 2009 regarding conception prior to August 1, 2002 of the use of an anti-Discoidin Domain Receptor 1 (DDR1) antibody, as recited in claims 17 and 18, to activate DDR1 and to induce the maturation of an immature macrophage or an immature dendritic cell. Exhibits A and B were attached to the declaration showing conception and due diligence until reduction to practice no later than August 14, 2002.
4. Claims 15 and 16 depend on cancelled claim 14. Accordingly, claims 15 and 16 have are withdrawn from consideration and not been treated further on the merits.

5. Note that the claims are examined to the extent that they read on the elected species: granulocyte-macrophage-colony stimulating factor as the DDR1-activating agent inducing expression of DDR1 (claims 13 and new claim 58) and a CD-40 ligand as the additional agent that enhances macrophages or dendritic cell maturation (claim 20). Note that because the genus claim is not allowable as originally claimed, no other species will be rejoined for search and examination.
6. Therefore, Claims 11-13, 17-25 and 55-59 are currently under examination to which the following grounds of rejection are applicable.

Response to Applicants' arguments

Withdrawn Rejections/Objections in response to Applicants' arguments or amendments

Claim Rejections - 35 USC § 112- Second Paragraph

In view of Applicants' amendment of claim 12, rejection of claim 12 under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language, has been withdrawn.

In view of Applicants' cancellation of claim 14, rejection of claim 14 under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language, is rendered moot.

Rejections/Objections maintained in response to Applicants' arguments or amendments

Claim Rejections - 35 USC § 103

Claims 11-13, 17-25, 55, and 57 remain rejected and new claims 58 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Radziejewski et al., (US Patent 6,022,694, Date of Patent Feb 8, 2000), in view of Lipford et al., (US Pub No. 2003/0148316, Date of Publication August 7, 2003).

Insofar as rejection of claims 58 and 59 under 35 U.S.C. 103(a) as being unpatentable over Radziejewski et al., and Lipford et al., Radziejewski discloses methods for promoting the growth, proliferation, differentiation, and/or survival of cells that express in their surfaces a receptor-like tyrosine kinase as Discoidin Domain Receptor (DDR1) comprising contacting the cell that expresses the DDR1 receptor with a DDR-1-activating agent (col. 12, lines 66-67, bridging to col. 13; col. 15, lines 24-31; col. 24, lines 15-17). Radziejewski discloses that COS cells used to express the DDR1 receptor were cultured in 10% BCS/DMEM. Thus any of the protein components in the serum is inherently a DDR1- activating agent **(Current claim 11).** In addition, Radziejewski discloses that subsequently, after serum removal from the medium, cells expressing DDR1, were further contacted with collagen to induce expression of DDR1 (col. 15, lines 33-35) **(Current claims 12 and 19).** Thus Radziejewski clearly discloses induction of DDR1 expression in DDR1 expressing DDR1 cells with a DDR1-activating agent such as serum proteins in the culture medium and further contacting with a DDR1-activating agent such as collagen to induce expression of DDR1, thus promoting cell growth, proliferation and differentiation of DDR-1 expressing cells. Lipford et al., complements the teachings of Radziejewski by disclosing maturation of dendritic cells from PBMC by treatment with GM-CSF and IL-4 (p.1, [004] [005]) **(Current claims 13 and 58).** Moreover, Lipford et al., teaches that

maturation of dendritic cells to professional APCs can be initiated by T cells expressing CD40 ligand (CD40L)(col. 1, [0004]) **(Current claims 20 and 59).**

Response to Applicants' Arguments as they apply to rejection of claims 11-13, 17-25, 55, 57, 58 and 59 under 35 USC § 103

At page 10 of the Remarks filed on 04-14-2009, Applicants essentially argue that Lipford et al., (US Pub No. 2003/0148316, Date of Publication August 7, 2003) filed on Aug. 1, 2002, claims priority to provisional application No. 60/309,260, filed on Aug. 1, 2001. However, Applicants allege, "Provisional Application No. 60/309,260 does not disclose DDR1 (or Accession No. U48705 or CD167a), nor does it disclose DDRl-activating agents, including antibodies that stimulate or induce dendritic cells. Accordingly, the priority date of Lipford et al., with respect to (i) DDR1, (ii) DDRl-activating agents, and (iii) antibody stimulation of dendritic cells, is August 1, 2002". Hence, Applicants contend that Lipford is improperly cited against claims 11-16, 19-25, 55 and 57. Moreover, Applicants argue that Radziejewski does not teach differentiation of macrophages or dendritic cell. The above arguments have been fully considered but deemed unpersuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Regarding (i), Lipford explicitly discloses DDR1 as one of the markers expressed in dendritic cells in US provisional application No. 60/309,260, filed on Aug. 1, 2001. See, for examples, documents filed on 08-01-2001, at page 788 of 815 filed, column 1, 4th row. See also

page at 606 evidencing filing date of deposit on August 1, 2001. Accordingly, the effective filing date for the DDR1 marker in dendritic cell is Aug. 1, 2001 and not August 1, 2002.

Regarding (ii), Radziejewski unambiguously discloses that COS cells expressing the DDR1 receptor were cultured in 10% BCS/DMEM. Thus any of the proteins in the serum is inherently a DDR1- activating agent, absent evidence to the contrary.

With respect to applicants' argument (iii) that, Provisional Application No. 60/309,260 does not disclose antibody stimulation of dendritic cells, thus priority date for the limitation of "antibody stimulation of dendritic" cells is August 1, 2002" is not found persuasive because it is noted that the features upon which applicant relies (i.e., antibody stimulation of dendritic cells) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). This is the case here. Claims 11-16, 19-25, 55 and 57 do not recite that limitation. Hence the argument is not persuasive as they argue limitations that are not present in the claims.

At pages 11 and 12 of Remarks, Applicants essentially argue that: 1) Exhibits A and B demonstrate that the subject matter of claims 17 and 18 was conceived prior to the August 1, 2002 filing date of Lipford et al., 2) Exhibit B specifically discloses in Fig. 12 that DDR-1 activating anti-DDR1 antibody was used to change the morphology of PMC cell, increase release of monocyte chemoattractant protein (MCP-1) from PMN and that both morphological changes and MCP-1 secretion are indicative of cell maturation, 3) that Lipford by disclosing a single anti-DDR1 activating antibody sufficiently anticipates the entire genus of anti-DDR1, particularly

because the antigen DDR1 was known. The above arguments have been fully considered but deemed unpersuasive.

Regarding 1) this is not disputed. However, as set forth in the paragraph above, the effective filing date for the DDR1 marker in dendritic cell in US Patent Application No. 10/212,133 is Aug. 1, 2001 and not August 1, 2002.

Regarding 2) and 3), one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. Claim 17 and 18 are rejected under 35 USC § 103 **o**ver Radziejewski et al., and Lipford et al.,

Radziejewski clearly discloses methods for promoting the growth, proliferation, differentiation, and/or survival of cells that express in their surfaces a receptor-like tyrosine kinase as Discoidin Domain Receptor (DDR1) comprising contacting the cell that expresses the DDR1 receptor with a DDR-1-activating agent and further contacting with collagen to induce expression of DDR1. Furthermore, Radziejewski clearly teaches binding agents to DDR1, which include antibodies specific for *in vitro* screening of cell lines that expressed DDR1. Lipford et al., complements the teachings of Radziejewski by disclosing maturation of dendritic cells from PBMC by treatment with GM-CSF and CD40 ligand (see US Patent Application No. 10/212,133 is Aug. 1, 2001, at pages 1 and 2, for example). Note that at the time the invention was made, the maturation of DC by contacting with GM-CSF, IL-4 and collagen was well known in the art as evidence by the teachings of Brand (*Eur J of Immunol.*, Pages 1673 – 1680; Abstract, of record).Hence Applicant has presented insufficient evidence commensurate with the scope of the claims, to rebut the combination of Lipford et al., Radziejewski., rendering obvious the instant

claims with respect to a method of inducing maturation of an immature dendritic cell that expresses DDR1 by contacting said dendritic cell with a DDR1-activating agent.

Claim 56 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Radziejewski et al., (US Patent 6,022,694, Date of Patent Feb 8, 2000), in view of Lipford et al., (US Pub No. 2003/0148316, Date of Publication August 7, 2003) a applied to claims 11-25, 55, and 57 above, and further in view of Vogel et al., (WO 98/34954; Date of Patent 13 August 1998).

Response to Applicants' Arguments as they apply to rejection of claim 56 under 35 USC § 103

At page 12, Applicants argue that claim 56 has an effective priority date of May 15, 2002, which predates the August 1, 2002 filing date of Lipford et al. Thus, Lipford et al. is improperly cited against claim 56. Such is not persuasive.

As set forth in the paragraph above, Lipford et al. specifically discloses maturation of dendritic cells expressing DDR1 from PBMC by treatment with GM-CSF. Thus the effective filing date for the DDR1 marker in dendritic cell in US Patent Application No. 10/212,133 is the earliest filing date of Aug. 1, 2001 and not August 1, 2002.

New Grounds of Rejection

Claim Rejections - 35 USC § 112- First paragraph- New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12, 13 and 57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection necessitated by amendment of the claims in the response filed 04-14-2009.**

Claim 12 recites "with an agent that up-regulates the expression of DDR1" . Likewise, **claim 13** recites the limitation "with an agent that up-regulates the expression of DDR1". Applicants cite page 46, line 25 through page 47, line 11, of the specification, for support of the limitation. The specification discloses at pages 47-48 regulation of DDR1 mRNA expression in PBMC and PMN by exogenous and endogenous proinflammatory agents. There are no indications where support may be found for the above limitations regarding up-regulation of DDR1 expression, however. A review of the specification as filed reveals no specific disclosure of up-regulation of DDR1 on immature dendritic cells or immature macrophages. What the specification does disclose regarding that DDR1 expression being up-regulated is that "activation of monocytes with GM-CSF, or lymphocytes with PHA, increased the DDR1 protein expression by each cell type, indicating that DDR1 expression can be up-regulated in both monocytes and lymphocytes (page 49, lines 19-23)". Note that dendritic cells and macrophages are not monocytes or lymphocytes. There is nothing more to lead one of skill in the art to appreciate that contacting an immature dendritic cells or immature macrophage expressing

DDR1 with an agent that up-regulates the expression of DDR1 induces maturation of an immature dendritic cells or immature macrophage. There is not discussion that the upregulation of mRNA DDR1 in PBMC resulted in upregulation of levels of DDR1 protein expression. Also note that up regulation of DDR1 mRNA expression in PBMC and PMN does not necessarily lead to upregulated expression of the corresponding protein as degradation by RNAses may result in reduced protein expression, for example. Thus the specific embodiments regarding the breadth of up-regulation of DDR1 expression on immature dendritic cells or immature macrophages sets forth a new range not previously disclosed as a contemplated embodiment in the present specification, or one that was readily known and used in the art at the time of filing. Hence, is not clear that the Applicant was in possession of a genus of undefined agents that up-regulates the expression of DDR1 in an immature dendritic cells or immature macrophage expressing DDR1. Furthermore, **claim 57** has been amended to recite "up-regulates chemokines or cytokines". Support for expression and secretion of chemokines, cytokines and proteases in the process of DC maturation, is found at page 12, lines 8-11 and at page 13, line 3. However, there is nothing to lead one of skill in the art to appreciate that contacting an immature dendritic cells or immature macrophage expressing DDR1 with a DDR1-activiting agent up-regulates chemokines or cytokines by a genus of undefined methods (e.g., upregulation of mRNA expression, cell surface protein expression or protein secretion) other than by expression and secretion of chemokines or cytokines. Thus, the amended claims include impermissible New Matter.

Response to Applicants' note to the Examiner

At page 13 of Remarks, Applicants essentially allege that two post-filing publications by Matsuyama et al., have been retracted by inventor Yoshimura leading to deletion of the limitation "up-regulates cell surface proteins" in claim 57, as results of Examples 2 and 4, supporting the deleted limitation are measured by flow cytometry which data may be flawed.

Note that amended claim 57 has been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement because there is not sufficient disclosure for up-regulation of chemokines or cytokines. There is nothing to lead one of skill in the art to appreciate that contacting an immature dendritic cells or immature macrophage expressing DDR1 with a DDR1-activiting agent up-regulates chemokines or cytokines by a genus of undefined methods other than by expression and secretion of chemokines or cytokines. Also note that claim 56 reads on activation of intracellular molecules comprising p38 MAP kinase by DDR1-induced activation in DC, which finds support in the specification as filed, Example 4 (See, page 79, lines 20-30, for example). However, the claim does not recite any flow cytometry determination of cell surface markers.

The following are cited to complete the record

Pages 606 and 788 of US provisional application No. 60/309,260 filed on Aug. 1, 2001.

Conclusion

Claims 11-13, 17-25 and 55-59 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of

document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

/Maria Leavitt/

Maria Leavitt, PhD
Examiner, Art Unit 1633